

**REMARKS**

The above amendments have been provided based on the format described at 1265 Off. Gaz. Pat. Office 87 (December 17, 2002) and as authorized by Deputy Commissioner for Patents, Stephen Kunin on January 31, 2003.

Claim 1 has been amended to incorporate language from claim 2 to better tailor the claims to encompass commercially contemplated embodiments of the invention. Claim 1 has also been amended to correct a clerical error in the omission of "acid" in line 4 of the claim. Additional support for the incorporation of language from claim 2 is provided at least by Figure 1 of the instant application. The amendment has been made for reasons related to business considerations rather than in acquiescence to any position set forth in the Office Action mailed March 26, 2003. Applicants reserve the right to pursue the subject matter of claim 1 as originally filed in a continuing application.

Claim 7 has been re-written in independent form to emphasize the subject matter being claimed and the distinction from the references cited in the Office Action mailed March 26, 2003. New claims 16-21, correspond to the subject matter of claims 7, 8, 5, 10, 12, and 15 respectively. They have been introduced to present the subject matter of claims 7, 8, 5, 10, 12, and 15 in combination with scope of amended claim 1.

No new matter has been introduced, and entry of the amendments is respectfully requested.

***Drawings***

The drawings were objected to as detailed in form PTO-948. Revised drawings are attached to the instant response and their entry as substitutes for the drawings of record has been presented above. Consideration of the revised drawings and withdrawal of the objection are respectfully requested.

***Rejections under 35 U.S.C. § 102***

Claims 1-6, 11-13, and 15 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Yu et al. (J. Virol. 1996, 70:4530-4537). Applicants have carefully reviewed the cited reference and statement of the rejection and traverse as follows with respect to the claims as amended.

Claim 1 is now directed to a packaging cell wherein the first nucleic acid construct comprises a tetracycline regulated promoter/operator. The cells of Yu et al., however, are HtTA-1 cells that comprise a corresponding first nucleic acid construct (pUHD15-1 as shown in Figure 1) which does not comprise a tetracycline regulated promoter/operator. Yu et al. refer to a reference 15 (see page 4533, left col., first complete sentence), which is Gossen et al. (PNAS 1992, 89:5547-5551), a copy of which is attached hereto. Gossen et al. teach that pUHD15-1 has the tTA sequence “under the control of the  $P_{hCMV}$  (human cytomegalovirus promoter IE” as noted on page 5547, right col., first paragraph of “Materials and Methods”.

A form PTO-1449 listing Gossen et al. is also attached hereto. Applicants respectfully request that the form be initialed and returned to make Gossen et al. of record in the instant application.

Because the HtTA-1 cells of Yu et al., containing a  $P_{hCMV}$  promoter in pUHD15-1, is not within the scope of claim 2 as originally filed, there is no *prima facie* case of anticipation of the claims as amended. Anticipation requires that every element of a claimed invention be disclosed by a single reference (see MPEP 2131 and the decisions cited therein). This standard has not been met by the application of Yu et al. against original claim 2, now amended claim 1. Therefore, Applicants respectfully submit that the instant rejection is misplaced and that this rejection may be properly withdrawn.

Claims 1, 3-8, and 10-15 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kafri et al. (J. Virol. 1999, 73:576-584). Applicants have carefully reviewed the cited reference and statement of the rejection and traverse as follows with respect to the claims as amended.

As an initial matter, the instant rejection failed to present a *prima facie* case of obviousness with respect to the original claims of the instant application for a simple reason. Kafri et al. disclose the use of ptTA $\Delta$ n to express tTA as a fusion with the C-terminal activation domain of VP-16. The fusion protein then regulates TRE mediated expression of VSV G protein, on plasmid pBIGFVG, and HIV encoded proteins, on plasmid pPTk. Therefore, if ptTA $\Delta$ n is the first construct as recited in the pending claims, there is no second construct that expresses a second gene product that regulates expression of a viral gene product encoded by a third construct as required by the claims. This follows because both plasmids pBIGFVG and pPTk encode viral gene products under the control of the fusion protein expressed by ptTA $\Delta$ n. Where is the second construct that expresses a second gene product to regulate expression of a viral gene product by a third construct?

The statement of the rejection appears to assert that the tat protein expressed by pPTk regulates expression of blue fluorescent protein (BFP) from the LTR promoter on a separate pLBFPL vector, but of course BFP, a variant of green fluorescent protein (GFP), is not a viral gene product.

As noted above, anticipation requires that every element of a claimed invention be disclosed by a single reference (see MPEP 2131 and the decisions cited therein). Therefore, and contrary to the statement of the rejection, Kafri et al. cannot anticipate the claims of the instant application, either as originally filed or as amended.

With respect to the claims as amended, Applicants point out that claim 1 is now directed to a packaging cell wherein the first nucleic acid construct comprises a tetracycline regulated promoter/operator. The cells of Kafri et al., however, are SODk0 cells that comprise a corresponding first nucleic acid construct (ptTA $\Delta$ n) which does not comprise a tetracycline regulated promoter/operator (see page 577, left col., first five sentences; and right col., first

paragraph of “Results”). Kafri et al. describe ptTA $\Delta$ n as expressing “the carboxy terminus of the tetracycline repressor and the herpes simplex virus VP16 transactivation domain … under the control of the CMV promoter” (*Ibid* and see page 576, right col., “Materials and Methods”).

Because the SODk0 cells of Kafri et al., containing a CMV (cytomegalovirus) promoter in ptTA $\Delta$ n, is not within the scope of claim 2 as originally filed, there is no *prima facie* case of anticipation of claim 1 as amended.

In light of the above, no case of anticipation has been presented by the application of Kafri et al. against the claims as originally filed or as now amended. Therefore, Applicants respectfully submit that the instant rejection is misplaced and that this rejection may be properly withdrawn.

#### ***Rejection under 35 U.S.C. § 103(a)***

Claims 1-6, 9, 11-13, and 15 have been rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Yu et al. (as cited above) in view of Ghosh et al. (J. Mol. Biol. 1993, 234:610-619). Applicants have carefully reviewed the cited reference and statement of the rejection and traverse as follows with respect to the claims as amended.

As an initial matter, the rejection appears to be directed to the scope of the claimed invention wherein one of the products of the first, second or third nucleic acid constructs is a fusion comprising the tetracycline repressor (tTA) and the tat activation domain. While Applicants appreciate the recognition that the scope of the claims encompasses such embodiments of the invention, the rejection does not appear to be directed at the specific language of any of the claims as filed or amended. If the instant rejection is maintained and is directed to the specific language of a pending claim, Applicants respectfully request that this be made clear in the next communication.

Turning to the statement of the rejection, Applicants respectfully point out that regardless of the alleged obviousness of substituting a Tat activation domain for the VP16 activation domain in

a fusion protein with tTA (asserted as based on Ghosh et al.), no *prima facie* case of obviousness with respect to original claim 2 and amended claim 1 has been presented for the reasons discussed above with respect to Yu et al.

Yu et al. fail to teach or suggest a packaging cell as encompassed by original claim 2 or amended claim 1 because they provide no disclosure or guidance concerning the use of a tetracycline regulated promoter/operator in the first nucleic acid construct as recited in the claims. Ghosh et al. fail to correct this deficiency because they also provide no disclosure or guidance concerning the use of a tetracycline regulated promoter/operator.

In light of the insufficiencies of the cited references, Applicants respectfully submit that the instant rejection is misplaced and that the rejection may be properly withdrawn.

Last, Applicants respectfully disagree with the assertion of Yu et al. and Ghosh et al. being “analogous art because they are from the same field of endeavor.” This is based upon the simple observation that while Yu et al. is directed to packaging cell lines for viral vectors, Ghosh et al. is directed to transcriptional regulation and the “synergism between Tat and VP16”. Contrary to the position in the statement of the rejection, the fields of packaging cells and transcriptional regulation are distinct rather than analogous.

Claims 1, and 3-15 have been rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Kafri et al. (as cited above) in view of Ghosh et al. (as cited above). Applicants have carefully reviewed the cited reference and statement of the rejection and traverse as follows with respect to the claims as amended.

As an initial matter and discussed above, Kafri et al. fail to teach or suggest the presence or use of a second nucleic acid construct encoding a product that regulates the expression of a **viral** gene product from a third nucleic acid construct. Ghosh et al. provide no teaching or suggestion to cure this defect. Accordingly, no *prima facie* case of unpatentability is present in a combination of Kafri et al. and Ghosh et al.

Moreover, the rejection appears to be directed to the scope of the claimed invention wherein one of the products of the first, second or third nucleic acid constructs is a fusion comprising the tetracycline repressor (tTA) and the tat activation domain. Thus, the rejection does not appear to be directed at the specific language of any of the claims as filed or amended. If the instant rejection is maintained and is directed to the specific language of a pending claim, Applicants respectfully request that this be made clear in the next communication.

Furthermore, Applicants respectfully point out that regardless of the alleged obviousness of substituting a Tat activation domain for the VP16 activation domain in a fusion protein with tTA (asserted as based on Ghosh et al.), no *prima facie* case of obviousness with respect to original claim 2 and amended claim 1 has been presented.

Kafri et al. fail to teach or suggest a packaging cell as encompassed by original claim 2 or amended claim 1 because they provide no disclosure or guidance concerning the use of a tetracycline regulated promoter/operator in the first nucleic acid construct as recited in the claims. Ghosh et al. fail to correct this deficiency because they also provide no disclosure or guidance concerning the use of a tetracycline regulated promoter/operator.

In light of the above and the insufficiencies of the cited references, Applicants respectfully submit that the instant rejection is misplaced and that the rejection may be properly withdrawn.

Last, Applicants respectfully disagree with the assertion of Kafri et al. and Ghosh et al. being “analogous art because they are from the same field of endeavor.” This is based upon the simple observation that while Kafri et al. is directed to packaging cell lines for viral vectors, Ghosh et al. is directed to transcriptional regulation and the “synergism between Tat and VP16”. Contrary to the position in the statement of the rejection, the fields of packaging cells and transcriptional regulation are distinct rather than analogous.

### CONCLUSION

In light of the above discussion, Applicants respectfully submit that the claims are allowable, and passage of the application to issue is urged. The Examiner is welcome to contact the undersigned if further discussions may be thought useful.

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Respectfully submitted,

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